REMARKS

Claims 51 and 57 are pending in the subject application. Applicants have not amended, cancelled or added any claims herein.

Rejection Under 35 U.S.C. §112, First Paragraph

In the March 11, 2008 Office Action, the Examiner rejected claims 51 and 57 as allegedly failing to comply with the written description requirement. The Examiner asserted that applicants were not in possession of an antibody "that has the ability to both bind to CCR5 and inhibit HIV fusion to cells because the specification fails to describe any monoclonal antibody that possess[es] such functions and fails to fully characterize the epitope(s) (or antigen) on CCR5 that are involved in HIV fusion to CD4". The Examiner also stated that "lacking knowledge of the specific epitope(s) on CCR5 that are required for HIV entry either in the prior art or the specification, one of ordinary skill in the art cannot envision what the monoclonal antibody is that inhibits HIV fusion even when accompanied by a method of making a monoclonal antibody to CCR5."

In response, applicants respectfully traverse the Examiner's ground of rejection and maintain that claim 51 and claim 57 dependent thereon satisfy the written description requirement of 35 U.S.C. §112, first paragraph.

Applicants note that the Court of Appeals for the Federal Circuit specifically addressed the question of adequate written description in the context of a claimed antibody in *Noelle v. Lederman*, 355 F.3d 1343, 1349, 69 USPQ2d 1508, 1514 (2004). In *Noelle*, the Court stated that disclosure of an antigen fully characterized by its structure, formula, chemical name, physical properties, or deposit in a public

depository provides an adequate written description of an antibody claimed by its affinity to that antigen.

Applicants maintain that the invention as recited in amended claim 51 describes an isolated antibody *which binds to a human CCR5 chemokine receptor on the surface of a CD4+ cell.* Moreover, applicants note that the antigen to which the antibody binds is well characterized. As the Examiner previously acknowledged on page 4 of the June 15, 2006 Final Office Action, the human CCR5 chemokine receptor sequence was in the public domain at the time of filing. Applicants further note that page 33, lines 3-17 and page 34, lines 23-30 of the specification describe the expression of the human CCR5 receptor in a CD4+ cell. As stated in M.P.E.P. §2163(II)(A)(3)(a)(1), "Information which is well known in the art need not be described in detail in the specification. See, e.g., *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986)." (emphasis added). In addition, M.P.E.P. §2163(II)(A)(2), citing *Vas-Cath* [supra], indicates that "if a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the written description requirement is met." Accordingly, consistent with *Noelle*, applicants maintain that the specification provides an adequate written description for the claimed antibody defined by its binding to a well known and fully characterized antigen, i.e. the human CCR5 chemokine receptor on the surface of a CD4+ cell.

Furthermore, raising antibodies against a known antigen was routine at the time of applicants' invention. The specification discloses how to obtain the sequence of CCR5, which was already known in the art as of the effective filing date of the subject application. The specification also discloses how to make the claimed antibodies by expressing on the surface of a CD4+ cell the human CCR5 chemokine

receptor protein encoded by the CCR5 nucleic acid sequence, and then using the resulting transfected, CCR5-expressing cells as immunogen to generate antibodies by routine methods well known in the art. Applicants further note that the claimed monoclonal antibody "binds to a human CCR5 chemokine receptor on the surface of a CD4+ cell" (emphasis added), which is a narrower genus than an antibody that binds to a CCR5 chemokine receptor polypeptide. In addition, as stated above, the specification discloses that the claimed antibody inhibits the fusion of HIV-1 to CD4+/CCR5+ cells. Moreover, the claimed antibody inhibits fusion of HIV-1, or an HIV-1 infected cell, to the CD4+ cell, so as to thereby inhibit HIV-1 infection of the CD4+ cell, wherein the CD4+ cell may be any of a PM-1 cell, a primary CD4+ T-cell, or a peripheral blood mononuclear cell (PBMC) as described in the specification. Applicants maintain that the genus described by these characteristics is adequately described in the specification.

With regard to the Examiner's assertion that the specification does not describe an antibody that "that has the ability to both bind to CCR5 and inhibit HIV fusion to cells because the specification fails to describe any monoclonal antibody that possess[es] such functions and fails to fully characterize the epitope(s) (or antigen) on CCR5 that are involved in HIV fusion to CD4", applicants point out that the specification, *inter alia*, at page 22, lines 8-30, discloses CD4+ mammalian cells incapable of fusing with Hela-env_{JR-FL} or Hela-env_{LAI} cells prior to expressing the human CCR5 chemokine receptor on their surface. After the human CCR5 chemokine receptor is expressed on their surface, such CD4+ cells are then able to fuse to Hela-env_{JR-FL} or Hela-env_{LAI} cells. The specification also discloses at page 31, lines 6-11 and in Table 3, that expression of the human CCR5 chemokine receptor in Hela-CD4+ cells rendered these cells readily infectible by primary HIV-1 strains in the env-complementation assay of HIV-1 entry, thus establishing that CCR5 is necessary for HIV-1 infection of these CD4+ cells.

Thus, applicants maintain that the specification adequately describes the claimed genus of antibodies to CCR5. The identifying characteristics and common attributes of the genus of claimed antibodies in claim 51 is adequately disclosed in the specification. The common features of the claimed genus are (1) binding to the human CCR5 chemokine receptor on the surface of a CD4+ cell, and (2) inhibiting fusion of HIV-1, or a HIV-1-infected cell, to such a CD4+ cell. Indeed, the specification also discloses, *inter alia* at page 28, line 23 to page 29, line 7 and Table 2, that the claimed antibodies have an inhibitory effect on fusion between CD4+/CCR5+ cells, e.g. PM1 cells, and Hela-env_{JR-FL}, but have no inhibitory effect between such cells and Hela-env_{LAI}, thus confirming the specificity of the fusion process.

The disclosed identifying characteristics and common features of the claimed antibodies, coupled with the high level of skill in the art as of the effective filing date of the subject application, provide an adequate written description for the claimed genus. Accordingly, applicants respectfully request reconsideration and withdrawal of this ground of rejection.

Rejection Under 35 U.S.C. §102(e)

The Examiner rejected claims 51 and 57 as anticipated by Li et al. (U.S. Patent No. 6,759,519) as evidenced by Wu (U.S. Patent 6,528,625).

In response, applicants respectfully traverse the Examiner's rejection. For a rejection under 35 U.S.C. §102(e) to be proper the alleged anticipatory prior art must teach each and every element of the claimed invention. However, there is no teaching in Li et al. of "an isolated monoclonal antibody which binds to a human CCR5 chemokine

receptor on the surface of a CD4+ cell". It is noted that the Examiner states that Li et al. "disclose an antibody that binds to the native HDGNR10 (later designated CCR5)." However, there is no teaching of a monoclonal antibody that binds to a human CCR5 chemokine receptor *on the surface of a CD4+ cell*. In addition, there is no teaching in Li et al. of an isolated monoclonal antibody which "inhibits fusion of HIV-1, or an HIV-1 infected cell, to the CD4+ cell, so as to thereby inhibit HIV-1 infection of the CD4+ cell". The Examiner cites col. 12, lines 19-27 of Li et al. as teaching antibodies which are antagonists "of the HDGNR10 (CCR5) polypeptide." However, what the Examiner cites is a general discussion of G-protein receptor antibody antagonists and not a teaching of the element as recited in claim 51, which is an antibody that "inhibits fusion of HIV-1, or an HIV-1 infected cell, to the CD4+ cell, so as to thereby inhibit HIV-1 infection of the CD4+ cell".

The Examiner goes on to assert that "Li's antibody and monoclonal antibody against CCR5 appears to have the inherent ability to inhibit HIV fusion to CD4 cells." The Examiner then asserts that such is evidenced by Wu. However, Wu et al. is not available as prior art, having an earliest prior art date of October 28, 1996, which is after the earliest claimed benefit date of the subject application (April 2, 1996). Thus the antibody taught by Wu et al. is not relevant to the failure of Li et al. to teach the claimed antibody.

Moreover, with regard to inherent anticipation, "[t]he fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. In re Rijckaert, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993)", as cited in M.P.E.P. §2112. More specifically, "[t]o establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so

recognized by persons of ordinary skill. *Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.*' In re Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999)" (M.P.E.P. §2112) (emphasis added). Li et al. does not actually teach the claimed antibody, and the "missing descriptive matter" is clearly not "necessarily present in the thing described in the reference." Accordingly, the anticipation rejection based on inherency is improper should be withdrawn.

With regard to the Examiner's position that "in the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed antibodies are different from those taught by the prior art and to establish patentable differences", applicants note that for the burden to be on the applicant, the Examiner must first have made a proper anticipation rejection. However, in the present case the Examiner's rejection based on inherency is improper for the reasons stated above.

With regard to the Examiner's position that "the claimed monoclonal antibody against CCR5 is not patentably distinct from those disclosed by Li et al. because the prior art antibody and monoclonal antibody against CCR5 have (1) the same specificity (against the same antigen)", applicants note that, as asserted above, the claimed antibody "binds to a human CCR5 chemokine receptor *on the surface of a CD4+ cell*" (emphasis added). Such a monoclonal antibody is <u>not</u> taught in Li et al. Thus, Li et al. does not teach a monoclonal antibody having the same specificity against the same antigen.

Accordingly, applicants respectfully request reconsideration and withdrawal of this ground of rejection.

Rejection Under 35 U.S.C. §103(a)

Li et al. and Wu et al.

The Examiner rejected claims 51 and 57 as obvious over Li et al. (U.S. Patent No. 6,759,519) as evidenced by Wu et al. (U.S. Patent 6,528,625).

In response, applicants respectfully traverse the Examiner's rejection. Wu et al. is not available as prior art as explained hereinabove. Moreover, as stated in MPEP §2141.03 "[o]bviousness cannot be predicated on what is not known at the time the invention is made, even if the inherency of the feature is later established." Furthermore, the claimed invention is not obvious over Li et al. because Li et al. does not teach all of the elements of the claimed invention as explained hereinabove. Accordingly, applicants respectfully request reconsideration and withdrawal of this ground of rejection.

Cocchi et al., Samson et al. and Berger et al.

The Examiner also rejected claims 51 and 57 as obvious over Cocchi et al. (Science, 207:1811-1815 (1995)), Samson et al. (Biochemistry, 35:3362-3367 (1996)) and Berger et al. (U.S. Patent No. 6,197,578), citing the Berger et al. reference as analogous art.

The Examiner asserts that the combined teachings of Cocchi et al. and Samson et al. suggest to one of ordinary skill in the art that "blocking the CCR5 receptor on a CD4 cell would inhibit HIV infection." Applicants disagree that the disclosures of Cocchi et al. and Samson et al. provide one of ordinary skill in the art with such teaching or suggestion. While Cocchi et al. discloses that a combination of polyclonal neutralizing antibodies against MIP-1α, MIP-1β and RANTES affect the activity of these chemokines to block

infection by HIV, and Samson et al. discloses that MIP-1α, MIP-1β and RANTES are natural ligands for CCR5, nothing is disclosed in the two references to make obvious applicants' claimed monoclonal antibody which binds CCR5 on the surface of a CD4+ cell and, via this binding, inhibits (independently of any of the chemokine ligands) fusion of HIV-1, or of an HIV-1-infected cell, to a CD4+ cell so as to inhibit infection of the CD4+ cell by HIV-1.

Samson et al. is silent regarding antibodies to CCR5. Cocchi et al. discloses polyclonal goat IgG against the MIP-1α, MIP-1β and RANTES chemokines. According to Cocchi et al., only a combination of these polyclonal antibodies against all of the chemokines blocked an HIV suppressive effect in the cell culture assay disclosed in Cocchi et al. Cocchi et al. and Samson et al. teach that only a combination of polyclonal antibodies directed against all of MIP-1α, MIP-1β and RANTES can affect the suppressive activity of these chemokines against HIV and that these chemokines have agonist effects against human CCR5 expressed in a cell line. The references combined do not teach or suggest a monoclonal antibody which binds to CCR5 on the surface of a CD4+ cell and blocks fusion of HIV-1, or of an HIV-1 infected cell, to the CD4+ cell so as to inhibit HIV-1 infection of the CD4+ cell. In the absence of applicants' own disclosure it would not be apparent from the disclosures of Cocchi et al. and Samson et al. that a single monoclonal antibody that binds CCR5 on a CD4+ cell would inhibit HIV-1 fusion to the CD4+ cell, or would inhibit fusion of an HIV-1-infected cell to the CD4+ cell, so as to inhibit HIV-1 infection of the cell.

Furthermore, it would not be obvious to make monoclonal antibodies directed against human CCR5 based on Berger's disclosure of CXCR4, which is a different antigen. Cocchi et al. and Samson et al. in combination with Berger et al. do not cure this deficiency. The Examiner stated, *inter alia*, that the ordinary artisan "[w]ould [...] have a reasonable expectation of success [...] given the knowledge that

the antibody against CXCR4 chemokine receptor can block HIV fusion, as taught by Berger." As previously pointed out by applicants, the claimed antibody relates to CCR5 which is a co-receptor for macrophage-tropic HIV strains, whereas CXCR4 is a receptor for T-cell tropic HIV strains. There is no basis for the assertion that there is a "reasonable expectation of success" because the prior art discloses a different antibody against a different receptor that blocks fusion of a different HIV strain.

Moreover, although the Examiner stated that one of ordinary skill in the art "would recognize that the prior art anti-CXCR4 antibody against HIV fusion to CD4+ T cells and the claimed anti-CCR5 antibody against HIV fusion to CD4 cells are functional equivalents although they target different chemokine receptors on CD4 cells", this cannot be a basis for the obviousness rejection because it is a conclusion based on applicants' own disclosure regarding the characteristics of the described anti-CCR5 antibody and is not based on the prior art.

Accordingly, applicants respectfully request reconsideration and withdrawal of this ground of rejection.

Obviousness-Type Double Patenting Rejections

1. U.S. Patent No. 7,122,185

The Examiner maintained the provisional rejection of claims 51 and 57 as allegedly unpatentable on the ground of nonstatutory obviousness-type double patenting over claims 1-9 of U.S. Patent No. 7,122,185.

In response, applicants respectfully traverse this obviousness-type double patenting rejection. Applicants maintain that if upon consideration of this Communication the pending claims are otherwise deemed allowable, applicants will consider filing a Terminal Disclaimer.

2. U.S. Serial No. 11/804,746

The Examiner maintained the provisional rejection of claims 51 and 57 as allegedly unpatentable on the ground of nonstatutory obviousness-type double patenting over claims 78-97 of U.S. Serial No. 11/804,746.

In response, applicants respectfully traverse this obviousness-type double patenting rejection. Applicants maintain that if upon consideration of this Communication the pending claims are otherwise deemed allowable, applicants will consider filing a Terminal Disclaimer.

3. U.S. Serial No. 11/805,573

The Examiner maintained the provisional rejection of claims 51 and 57 as allegedly unpatentable on the ground of nonstatutory obviousness-type double patenting over claims 78-107 of U.S. Serial No. 11/804,746.

In response, applicants respectfully traverse this obviousness-type double patenting rejection. Applicants maintain that if upon consideration of this Communication the pending claims are otherwise deemed allowable, applicants will consider filing a Terminal Disclaimer.